EXHIBIT

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Transvaginal mesh or grafts compared with native tissue repair for vaginal prolapse (Review)

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[Intervention Review]

Transvaginal mesh or grafts compared with native tissue repair for vaginal prolapse

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ABSTRACT

Background

A wide variety of grafts have been introduced with the aim of improving the outcomes of traditional native tissue repair (colporrhaphy) for vaginal prolapse.

Objectives

To determine the safety and effectiveness of transvaginal mesh or biological grafts compared to native tissue repair for vaginal prolapse.

Search methods

We searched the Cochrane Incontinence Group Specialised Register, which contains trials identified from the Cochrane Central Register of Controlled Trials (CENTRAL), MEDLINE, ongoing trials registers, and handsearching of journals and conference proceedings *(6* July 2015*).* We also contacted researchers in the field.

Selection criteria

Randomised controlled trials (RCTs) comparing different types of vaginal repair (mesh, biological graft, or native tissue).

Data collection and analysis

Two review authors independently selected trials, assessed risk of bias, and extracted data. The primary outcomes were awareness of prolapse, repeat surgery, and recurrent prolapse on examination.

Main results

We included 37 RCTs (4023 women). The quality of the evidence ranged from very low to moderate. The main limitations were poor reporting of study methods, inconsistency, and imprecision.

Permanent mesh versus native tissue repair

- when these products are used correctly they can help alleviate the very distressing symptoms of stress urinary incontinence and pelvic organ prolapse, and as such the benefits still outweigh the risks.

Our review suggests that while permanent transvaginal mesh is associated with a greater reduction in prolapse on examination, awareness of prolapse and reoperation for prolapse than native tissue repairs, it is associated with increased morbidity, including a higher rate of bladder injury, de novo stress urinary incontinence, and reoperation rates for prolapse, stress urinary incontinence, and/or mesh exposure. The rate of mesh exposure was 12%, and surgery for mesh exposure was required in 8%, accounting for most of the reoperations for mesh complications. We conclude, in contrast to the MHRA 2014 report, that while there may be individual cases of anterior compartment prolapse where mesh utilisation may be warranted, it cannot be considered a first-line treatment option for pelvic organ prolapse, due to the associated morbidity.

Furthermore, and in contrast to the MHRA 2014 report, we have highlighted that most of data informing our report was derived from transvaginal mesh products that were voluntarily removed from the market in 2012, and that transvaginal mesh products currently available for use have not been evaluated by RCTs. We believe it is prudent that until such data become available, the currently available transvaginal mesh products should be utilised in a clinical setting under the discretion of the local ethics committee.

A recent Cochrane systematic review (Ford 2015) assessed mid-urethral sling operations for the treatment of women with stress urinary incontinence. It included comparisons of different surgical routes, different types of synthetic tape and types of tape insertion. The review authors concluded that the surgery has a good safety profile and is highly effective in the short and medium term. This review has limited applicability to the current review, as it included women with or without pelvic prolapse; most trials did not report whether prolapse was present. Moreover none of the trials directly compared traditional anterior repair (with native tissue) to mid-urethral synthetic sling.

AUTHORS' CONCLUSIONS

Implications for practice

While transvaginal permanent mesh is associated with lower rates of awareness of prolapse and prolapse on examination than native tissue repair, permanent mesh is also associated with increased morbidity, including a higher rate of reoperation for prolapse, stress urinary incontinence, or mesh exposure and higher rates of bladder injury at surgery and de novo stress urinary incontinence. The risk-benefit profile means that transvaginal mesh has limited utility in primary surgery. While it is possible that the benefits may outweigh the risks in women with higher risk of recurrence, there is currently no evidence to support this position.

Limited evidence suggests that absorbable mesh may reduce the risk of recurrent prolapse on examination compared to native tissue repair, but there was insufficient evidence on absorbable mesh for us to draw any conclusions for other outcomes.

In 2011, many of the transvaginal permanent meshes evaluated in this review were voluntarily withdrawn from the market. To date, the newer, lightweight transvaginal permanent meshes that remain of the market have not been evaluated within a RCT. Until such data become available, these newer transvaginal meshes should be utilised under the discretion of the ethics committee.

Implications for research

In the short term, urgent evaluation of newer, lighter transvaginal mesh products that remain on the market is required. Unfortunately, at least two trials have received ethical committee approval comparing the new lightweight mesh with either sacral colpopexy or transanal repair (NCT01097200; NCT01497171), but have been terminated due to difficulty in recruiting or lack of funding. These products should also be compared to native tissue repairs and sacral colpopexy. In the medium to long term, the development of newer, self rejuvenating products through tissue engineering and bio-design should be funded, and the efficacy, safety, and cost of the interventions assessed. A cost-benefit analysis of transvaginal mesh is needed, and the long-term outcomes of meshes already evaluated should also be undertaken.

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